UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,729	03/28/2002	Preeti Lal	PF-0687 USN	8120

27904 7590 01/27/2004

INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,729	LAL ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,15 and 20-29* is/are pending in the application.

4a) Of the above claim(s) *9,12 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,5,6,8,10,11 and 15* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-6, 8-12, 15, 20-29 are currently pending and are present for examination. Claims 1-6, 8, 10-11 and 15 are now under consideration. Claims 9, 12, 20-29 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election of Group V, claims 1-6, 8, 10-11 and 15 in Paper filed on 10-31-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Rejoinder of restricted inventions

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. **Thus, to be allowable, the rejoined claims must meet all criteria for**

patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims will be maintained. **Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.** See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to rejoin, in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

The listing of references in the specification (for example in Table 5) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (for example see p.12). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 recites the phrase "under conditions whereby a hybridizing complex is formed". The metes and bounds of the above phrase is not clear to the Examiner. It is not clear to the Examiner as to what specific hybridization conditions are contemplated by the applicant. This is because non-specific complexes are invariably formed under low stringency conditions that could lead to false signal.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 recites the phrase "an effective amount". The metes and bounds of the above phrase is not clear to the Examiner. In other words, the pharmaceutical composition comprises the polypeptide in an effective amount for what? Is it for treatment of a disorder or specific biological pathway etc.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 6, 8, 10-12, 15, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide with SEQ ID NO:10 and the encoded polypeptide with SEQ ID NO:5 having UDP-glucuronosyl transferase activity, vector and host cells transformed with said vectors and a method of making the polypeptide with SEQ ID NO:5, does not reasonably provide enablement for any naturally occurring polynucleotide having 70% sequence identity with SEQ ID NO:10 without any specific function associated with such polynucleotide or complementary polynucleotides of the same or a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:10 or a method of detecting a target polynucleotide having a sequence of the above polynucleotide or a polypeptide that is naturally occurring and having at least 90% sequence identity to SEQ ID NO:5 without any specific function associated with said polypeptide or a pharmaceutical composition comprising the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 3, 5, 6, 8, 10-12, 15 are so broad as to encompass any naturally occurring polynucleotide having 70% sequence identity with SEQ ID NO:10 or complementary polynucleotides of the same or a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:10 without any specific function associated with such polynucleotide or a method of detecting a target polynucleotide having a sequence of the above polynucleotide or a polypeptide that is naturally occurring and having at least 90% sequence identity to SEQ ID NO:5 without any specific function associated with said polypeptide or a pharmaceutical composition comprising the same. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single UDP-glucuronosyl transferase. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides with an undefined function/activity. The specification is limited to teaching the use of SEQ ID NO:5 as a UDP-glucuronosyl transferase and the polynucleotide with SEQ ID NO:10 as the sequence which can be used to encode or express the above polypeptide but provides no guidance with regard to the making and using of variants and mutants or with regard to other uses. In view of

the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all naturally occurring polypeptides having 90% amino acid sequence identity with SEQ ID NO:5 or all naturally occurring polynucleotides having 70% nucleic acid sequence identity with SEQ ID NO:10 because the specification does not establish: (A) any specific use for naturally occurring polynucleotides that have 70% sequence identity with SEQ ID NO:10; (B) any specific use for naturally occurring polypeptides that have at least 90% sequence identity with SEQ ID NO:5; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides and polypeptides with an enormous number of changes to SEQ ID NOS: 5 and 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, use of claimed polynucleotides and polypeptides is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 3, 5, 6, 8, 10-12, 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of naturally occurring polynucleotides and polypeptides having the limitations of being 70% identical to SEQ ID NO:10, vectors and host cells and method of using such polynucleotides and 90% identical to SEQ ID NO:5 and pharmaceutical composition comprising said polypeptides, respectively.

The specification does not contain any disclosure of the function of all polynucleotide sequences that are 70% identical to SEQ ID NO:10 or functions of all polypeptide sequences that are 90% identical to SEQ ID NO:5. The genus of polynucleotides and polypeptides that comprise or consist of these above polynucleotides and polypeptides molecules is a large variable genus with the potentiality of encoding many different proteins in case of

polynucleotides and with a potentiality of having different functions in case of polypeptides. Therefore, many functionally unrelated polynucleotides and polypeptides are encompassed within the scope of these claims, including partial polynucleotides and polypeptides sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Chowdhury et al. (Hepatology, (1984) Vol. 4, No. 5, pp. 1074.) or Pfeil et al. (European Journal of Biochemistry, (1983) Vol. 131, No. 3, pp. 619-624) or Mackenzie et al. (Journal of Steroid Biochemistry, (1983) Vol. 19, No. 2, pp. 1097-1102) or Jin CJ et al. (BBRC, 1993, Vol.

194(1):496-503). This rejection is based upon the public availability of a printed publication. Claims 1-2, 15 are drawn to an isolated polypeptide comprising the amino acid sequence with SEQ ID NO:5 having UDP-glucuronosyl transferase activity or a naturally occurring polypeptide having, an amino acid sequence that is at least 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same. All the four references above, Jin CJ et al., Chowdhury et al., Pfeil et al., Mackenzie et al., disclose an isolated and purified polypeptide having UDP-glucuronosyl transferase activity. However, the references do not disclose that said polypeptide has the amino acid sequence of SEQ ID NO:5 or that the amino acid sequence of said polypeptides are 90% identical to SEQ ID NO:5. However, because the polypeptides have identical activities, Examiner takes the position that a characteristic such as the amino acid sequence is an inherent characteristic of a given polypeptide and therefore the polypeptides of the references have either the same amino acid sequence as that of SEQ ID NO:5 or an amino acid sequence that at least 90% identical to SEQ ID NO:5. Therefore Jin CJ et al., Chowdhury et al., Pfeil et al., Mackenzie et al., anticipate claims 1-2, 15 as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claims 1, 3, 5-6, 8, 10-11, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Jackson et al. (Biochem. J., 1987, Vol. 242 :581-588 and Swiss Prot accession No. P06133). This rejection is based upon the public availability of a printed publication. Claims 1, 3, 5-6, 8, 10-11, 15 an isolated naturally occurring polypeptide having UDP-glucuronosyl transferase activity, an amino acid sequence that is at least 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or an isolated naturally occurring polynucleotide that is at least 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide. Jackson et al. (see also enclosed sequence alignments) disclose the isolation of such a naturally occurring polypeptide having UDP-glucuronosyl transferase activity, and an amino acid sequence that is more than 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or that is more than 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide. Therefore Jackson et al. anticipate claims 1, 3, 5-6, 8, 10-11, 15 as written.

Claims 1, 3, 5-6, 8, 10-11, 12, 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Galvin et al. (US 6586175, issued 7-1-03 and US 2003/0077629 A1, 4-24-03).

This rejection is based upon the public availability of a patent granted to another and a printed patent application publication. Claims 1, 3, 5-6, 8, 10-11, 12, 15 an isolated naturally occurring polypeptide having UDP-glucuronosyl transferase activity, an amino acid sequence that is at least 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or an isolated naturally occurring polynucleotide that is at least 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide, a method of detecting a target polynucleotide in a sample wherein in the target polynucleotide is one of the above polynucleotides using the method of hybridization. Galvin et al. disclose (see enclosed sequence alignments) the isolation of such a naturally occurring polypeptide having UDP-glucuronosyl transferase activity, and an amino acid sequence that is more than 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or that is more than 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide and a method of detecting a genetic polymorphisms in the target polynucleotide in a given sample using the method of hybridization. Therefore Galvin et al. anticipate claims 1, 3, 5-6, 8, 10-11, 12, 15 as written.

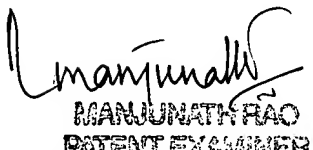
Conclusion

Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
January 14, 2004